44. The composition of claim 43, wherein said omega-6 polyunsaturated fatty acid is arachidonic acid.

New Matter

1. The examiner rejects claims 40 and 42-44 under 37 CRR 112(1) on an assertion that the claimed amount of bitter willow extract of 10-25 mg does not comport with the 10-50 mg range disclosed in the specification (p. 9, [029] and Example 17.

As long as a claimed range falls within the range disclosed in the specification, a rejection under 37 CFR 112(1) is improper. Nevertheless, in order to expedite allowance of the claims, claim 40 has been amended so as to recite the range of 10-50 mg recited in the specification.

2. The examiner also rejects all claims under 37 CFR 112(1) on an assertion that the specification does not disclose docosahexenoic acid, omega-6 polyunsaturated fatty acid and arachidonic acid.

The applicant respectfully submits that those skilled in the present art to whom this patent application is directed will readily understand what is encompassed by the term "polyunsaturated fatty acids", as used herein. To illustrate this, the applicant attaches several state-of-the art, publicly available references.

In an article by Drs. Dennis Lee and Gregory Thomas, published in MedicineNet.com, "polyunsaturated fatty acids" (PUFA) are broadly defined as fatty acids containing one than one double bond. Omega-3 and omega-6 are shown to be simply classes of PUFA, with the double bonds being in different locations in the carbon chain. Note also that fish oils are shown to be rich in these PUFAs.

In an article in PUFAs News from Harvard University, omega-3 PUFAs are well known to encompass docosahexenoic acid and eicosapentenoic acid.

In another article, this one from Everything2.com, it is shown that arachidonic acid is an omega-6 polyunsaturated fatty acid (eicosatetraenoic acid), whereas eicosapentenoic and docosahexenoic acids are known to be omega-3 polyunsaturated fatty acids. Also demonstrated is the fact that fish oils are rich in PUFAs.

Taken together, the evidence shows that those skilled in this art will readily understand that PUFAs encompass the compounds recited in the claims.

Double Patenting

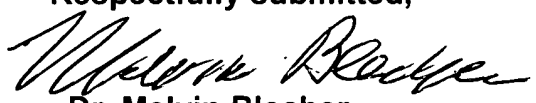
The examiner provisionally rejects claims 40-44 on an assertion of nonstatutory double patenting over claims 1,4,6,9,18, and 41-44 of copending Application No. 10/439,301. The '301 patent application is pending at this time or writing.

The applicant accepts the examiner's suggestion and is submitting herein a Provisional Terminal Disclaimer pursuant to 37 CFR 1.321 (b) and (c) over copending 10/439,301.

The application respectfully requests that all rejections now be withdrawn, and all claims passed to allowance and issuance expeditiously.

Respectfully submitted,

Date of signature: April 28, 2006



Dr. Melvin Blecher
Reg. No. 33,649

Law Offices of Dr. Melvin Blecher
4329 Van Ness St., NW
Washington, DC 20016-5625
Tel. 202 363 3338
FAX 202 362 8404
E MBiplaw@comcast.net

Doctor's Views

Fats, Fish Oil and Omega-3-Fat Acids

Medical Author: Dennis Lee, M.D.
Medical Author: Gregory Thomas, M.D.

Basics
- Healthy Recipes
- Stress Relief
- Weight Loss

Should You Know These Conditions?
- Multiple Sclerosis (MS)
- Diarrhea
- Breast Cancer
- Diabetes
- Hepatitis C

Services & Tools
Free Newsletters
Download (PDF) Reports
Audio Medical Podcasts
Find a Therapist by Psychology Today

Inside MedicineNet®
Meet the Doctors
Site Map

News & Information

What is fat?

Fat (also known as lipid), is one of the three class nutrients; the other two are proteins and carbohyd The major function of fat is to provide energy for t Pound per pound, fat contains more energy (calor than protein and carbohydrates. There are three t fat:

1. triglycerides,
2. cholesterol, and
3. phospholipids.

Triglycerides are where most of the fat calories ar stored. In addition to providing energy, fat also ser other functions, for example, cholesterol and phospholipids are components of cell membranes sheaths surrounding nerve cells. Cholesterol is al important for the production of bile acids and othe hormones (such as sex hormones and adrenal hormones).

What are fatty acids?

Fatty acids consist of chains of carbon atoms link together by chemical bonds. On one end (terminal carbon chain is a methyl group (a cluster of carbo hydrogen atoms), the other terminal is a carboxyl cluster of carbon, oxygen and hydrogen atoms). T

chemical bonds between carbon atoms can be eit single or double bonds. Single bonds have more hydrogen molecules around them than double bo These chemical bonds determine whether a fatty saturated or unsaturated (see discussion below). acids also come in different lengths: short chain fa acids have less than 6 carbons, while long chain f acids have 12 or more carbons.

Fatty acids serve as energy for the muscles, heart other organs, as building blocks for cell membran as energy storage for the body. Those fatty acids used up as energy are converted into triglycerides triglyceride is a molecule formed by attaching thre acids onto a glycerol compound that serves as a backbone. Triglycerides are then stored in the bo (adipose) tissue.

What are saturated fatty acids?

Saturated fatty acids contain single bonds only. F containing saturated fatty acids are called saturat Examples of foods high in saturated fats include l butter, whole milk, cream, eggs, red meat, chocol solid shortenings. Excess intake of saturated fat c one's blood cholesterol and increase the risk of developing coronary artery disease.

What are monounsaturated fatty acids?

Monounsaturated fatty acids contain one double b Examples of foods high in monounsaturated fat in avocados, nuts, and olive, peanut and canola oils. Scientists believe that increased consumption of monounsaturated fats (for example eating more n beneficial in lowering LDL cholesterol (the "bad" cholesterol) and lowering the risk of coronary hear disease, especially if monounsaturated fats are us

substitute for saturated fats and refined sugars.

What are polyunsaturated fatty acids?

Polyunsaturated fatty acids contain more than on bond. Examples of foods high in polyunsaturated f include vegetable oils, corn, sunflower, and soy.

What are essential fatty acids?

Essential fatty acids are polyunsaturated fatty aci the human body needs for metabolic functioning b cannot produce, and therefore has to be acquired food.

What are omega-3 fatty acids?

Omega-3 fatty acids are a class of essential polyunsaturated fatty acids with the double bond i third carbon position from the methyl terminal (he use of "3" in their description). Foods high in ome fatty acids include salmon, halibut, sardines, alba trout, herring, walnut, flaxseed oil, and canola oil. foods that contain omega-3-fatty acids include shr clams, light chunk tuna, catfish, cod, and spinach.

What are omega-6 fatty acids?

Omega-6 fatty acids are a class of essential polyunsaturated fatty acids with the initial double the sixth carbon position from the methyl group (h the "6"). Examples of foods rich in omega-6 fatty include corn, safflower, sunflower, soybean, and cottonseed oil.

What are the n-3 and n-6 fatty acids?

These are synonyms for omega-3 and omega-6 f acids, respectively.

What are trans fatty acids?

Trans fatty acids (trans fats) are made through hydrogenation to solidify liquid oils. Heating omeg such as corn oil to high temperatures creates tran Trans fats increase the shelf life of oils and are fo vegetable shortenings and in some margarines, commercial pastries, fried foods, crackers, cookie snack foods. Intake of trans fatty acids increases LDL-cholesterol ("bad" cholesterol), decreases H cholesterol ("good cholesterol"), and raises the ris coronary heart disease.

1 2 3 | Next ▸

Printer-Friendly Format | Email to a Friend Free Newsletter (Cholesterol Newsletter) Email a

Last Editorial Review: 2/1/2005

Polyunsaturated Fatty Acids (PUFAs)

Last updated: Wednesday, March 22, 2006

PUFAs News

PUFAs Links

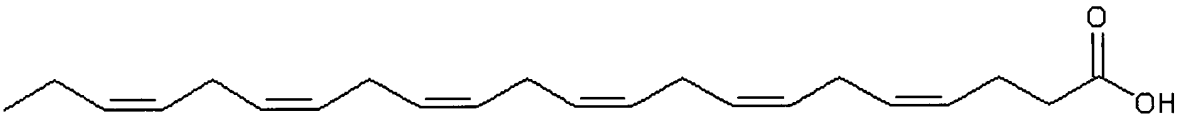
Cell membranes consist of a bilayer primarily composed of various phospholipids, cholesterol, and integral (imbedded) proteins that function as cell-surface receptors, enzymes, and various transporters. In the nervous system, cell membranes contain relatively high concentration of polyunsaturated fatty acids (**PUFAs**), such as **docosahexaenoic acid (DHA)**[1], which contains 22 carbons and six ***cis*** double bonds (see **Figure 1**). The fatty acid (**FA**) composition of phospholipids determines biophysical (and functional) characteristics of membranes (e.g., membrane "fluidity"), and plays an important role in cellular integrity, and intra and intercellular communication (signaling). Furthermore, there is abundant literature evidence (see below) that essential fatty acids (**EFAs**), and especially polyunsaturated fatty acids (**PUFAs**), play fundamental role in development and proper functioning of the nervous system; consequently, the **EFA** composition of membrane phospholipids likely plays a direct role in a variety of cellular and multicellular processes, including inflammation and immunity, with implications for neurodegenerative diseases. The links below provide recent literature overview of relevant topics.

Polyunsaturated Fatty Acids (PUFAs) References (644 References)

PUFAs Review References (405 References)

- **Docosahexaenoic acid (DHA)** (319 references)
- **Eicosapentaenoic acid (EPA)** (222 references)
- **PUFAs and dopamine** (23 References)
- **PUFAs and neurodegeneration** (17 References)
- **PUFAs and nitric oxide (NO)** (36 References)
- **PUFAs and Synuclein** (4 References)

[1]Docosahexaenoic acid or **DHA** is an omega-3 fatty acid with six ***cis*** double bonds and 22 carbons (22:6n-3).



Docosahexaenoic Acid (DHA) (22:6 n-3)

Figure by RMB

Figure 1. Chemical structure of docosahexaenoic acid (DHA). DHA is an omega-3 fatty acid with 22 carbons and six ***cis*** double bonds (22:6n-3).

Structure of DHA and EPA

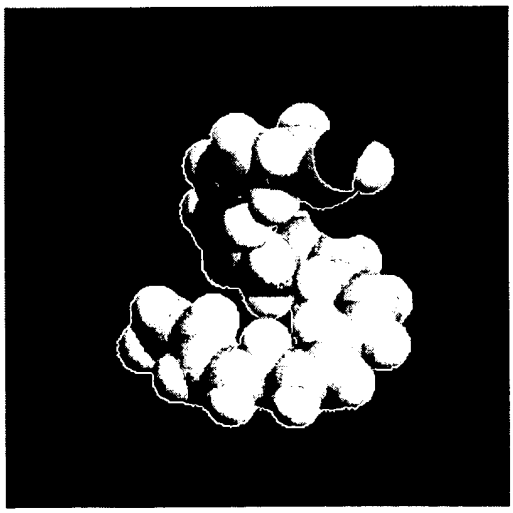


Figure 2. A 3-Dimensional model of Docosahexaenoic acid (DHA), depicting one potential conformation of DHA; due to the presence of six ***cis*** double bonds, DHA can assume a large number of highly bent conformers[2].

➡ Click on the above image thumbnail to see a larger image in a separate window.

[2]For a review of the unique properties of docosahexaenoic acid (DHA), see a review article: **"Docosahexaenoic acid: membrane properties of a unique fatty acid"** *Chemistry and Physics of Lipids* 126(2003) 1–27. Stillwell, W., and Wassall, S.R. ➡ Link to: **PubMed**

News

➡ **News:**

From MEDLINEplus News by Date:
MEDLINEplus: Fortified Foods Could Spread Fish Oil's Benefits
(Reuters Health; Friday, January 2, 2004)

Nutrition Source Web Site Offers the Latest News and Research on Diet and Health from Trusted Authority
(From the Department of Nutrition at the Harvard School of Public Health; Thursday, January 2, 2003)

➡ Links to other web sites of interest to PUFAs:

EFA Education

The Fish Foundation

Fish and Omega-3 Fatty Acids
(From **AHA** Recommendation)

International Society for the Study of Fatty Acids and Lipids

polyunsaturated fatty acid

(thing) by **peanut** (10.8 mon) (print) ? 1 **C!** Tue Jul 27 2004 at 22:15:56

Fatty acids are a simple lipid made up of a hydrophilic carboxylate group attached to a long hydrocarbon chain. These fatty acids are categorized as either saturated or unsaturated, depending on if all the carbons in the chain are fully bonded to hydrogen atoms (it is saturated with hydrogen) or if some carbons share bonds with each other (it is unsaturated). Polyunsaturated fatty acids, often abbreviated PUFAs, are fatty acids that have multiple (poly) double bonds in a cis configuration. These double bonds cause kinks in the normally straight hydrocarbon chain, which prevents the fatty acids from packing tightly together. The bends lowers the melting point of the fatty acid and causes it to be liquid at room temperature. Additional double bonds help to further lower the melting point.

Unlike monounsaturated and saturated fatty acids, the major polyunsaturated fatty acids cannot be synthesized by the body. They are therefore called "essential fatty acids" and must be consumed. The two major types of polyunsaturated fatty acids are linoleic acid and linolenic acid. Linoleic is an omega-6 fatty acid, meaning one of its double bonds is between the sixth and seventh carbon on the chain. It is the most abundant polyunsaturated fatty acid in human tissues and can be found in soybeans and in most vegetable oils including corn, sunflower, and safflower oil. Linolenic acid is an omega-3 fatty acid, meaning one of its double bonds is between the third and fourth carbons. This type is present in walnuts, soybeans, wheat germ, and flax, hemp, and pumpkin seeds.

There are also several types of important polyunsaturated fatty acid that can be synthesized from one of the two major fatty acids

described above. Linoleic acid can be turned into arachidonic acid, another omega-6 fatty acid. This fatty acid is also found in animal products such as liver and egg yolks. Linolenic acid can be converted into eicospentaenoic acid (EPA) and docosahexaenoic acid (DHA), both omega-3 fatty acids. Both can also be found in the oils of fish, especially salmon.

Polyunsaturated fatty acids are much more chemically reactive than monounsaturated or saturated fatty acids. Because of this oils that contain high levels of polyunsaturated fatty acids, such as soybean oil and corn oil, are much more prone to oxidation and spoilage. Manufacturers have been able to overcome this problem by hydrogenating the oil. Hydrogenation stabilizes the oil, increases its shelf life, and makes it solid at room temperature. This process forcibly adds hydrogen atoms to the double bonds in the carbon chain and converts the healthy unsaturated fatty acid back to an unhealthy saturated fatty acid. It also creates trans fatty acids, which are thought to be especially unhealthy.

Polyunsaturated fatty acids have a variety of functions in the body. They have been shown to effectively lower plasma cholesterol levels and are a common component of cell membranes. They also are important for the function of brain cells, nerves, adrenal glands, and certain hormones. Arachidonic acid is the building block for hormone-like molecules called eicosanoids. These molecules include prostaglandins, thromboxanes, prostacyclins and leukotrienes. They are involved in a wide variety of bodily functions including muscle movement, blood clotting, and the immune response. EPA helps to prevent the formation of blood clots that can lead to clogged arteries and also appears to lower levels of triglycerides, a risk factor in heart disease. DHA is important for lipid formation in the brain and the retina and is also converted into prostaglandins.

http://www.medicinalfoodnews.com/vol01/issue7/sat_fat.htm
http://www.lordsday.org/Fats.htm

Lipid compounds include monoglycerides, diglycerides, triglycerides

Fats, Oils, Fatty Acids, Triglycerides - Chemical Structure

Lipids consist of numerous fatlike chemical compound that are insoluble in water but soluble in organi solvents. Lipid compounds include monoglyceride diglycerides, triglycerides, phosphatides, cerebroside sterols, terpenes, fatty alcohols, and fatty acids. Dietar fats supply energy, carry fat-soluble vitamins (A, D, E K), and are a source of antioxidants and bioactiv compounds. Fats are also incorporated as structur components of the brain and cell membranes.

See also: PROTEINS/AMINO ACIDS
CARBOHYDRATES/SUGARS

Common Fatty Acids

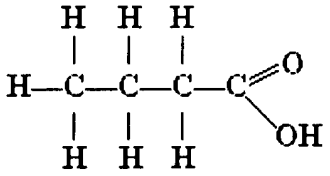
Chemical Names and Descriptions of some Common Fatty Acids

Common Name	Carbon Atoms	Double Bonds	Scientific Name	Source
Butyric acid	4	0	butanoic acid	butterfa
Caproic Acid	6	0	hexanoic acid	butterfa
Caprylic Acid	8	0	octanoic acid	coconu oil

Capric Acid	10	0	decanoic acid	coconut oil
Lauric Acid	12	0	dodecanoic acid	coconut oil
Myristic Acid	14	0	tetradecanoic acid	palm kernel oi
Palmitic Acid	16	0	hexadecanoic acid	palm oil
Palmitoleic Acid	16	1	9-hexadecenoic acid	animal fats
Stearic Acid	18	0	octadecanoic acid	animal fats
Oleic Acid	18	1	9-octadecenoic acid	olive oil
Vaccenic Acid	18	1	11-octadecenoic acid	butterfa
Linoleic Acid	18	2	9,12-octadecadienoic acid	grape seed oil
Alpha-Linolenic Acid (ALA)	18	3	9,12,15-octadecatrienoic acid	flaxseed (linseed) oil
Gamma-Linolenic Acid (GLA)	18	3	6,9,12-octadecatrienoic acid	borage oil
Arachidic Acid	20	0	eicosanoic acid	peanut oil, fish oil
Gadoleic Acid	20	1	9-eicosenoic acid	fish oil
Arachidonic Acid (AA)	20	4	5,8,11,14-eicosatetraenoic acid	liver fats

EPA	20	5	5,8,11,14,17-eicosapentaenoic acid	fish oil
Behenic acid	22	0	docosanoic acid	rapeseed oil
Erucic acid	22	1	13-docosenoic acid	rapeseed oil
DHA	22	6	4,7,10,13,16,19-docosahexaenoic acid	fish oil
Lignoceric acid	24	0	tetracosanoic acid	small amounts in most fats

Fatty acids consist of the elements carbon (**C**), hydrogen (**H**) and oxygen (**O**) arranged as a carbon chain skeleton with a carboxyl group (**-COOH**) at one end. **Saturated fatty acids** (SFAs) have all the hydrogen that the carbon atoms can hold, and therefore, have no double bonds between the carbons. **Monounsaturated fatty acids** (MUFAs) have only one double bond. **Polyunsaturated fatty acids** (PUFAs) have more than one double bond.

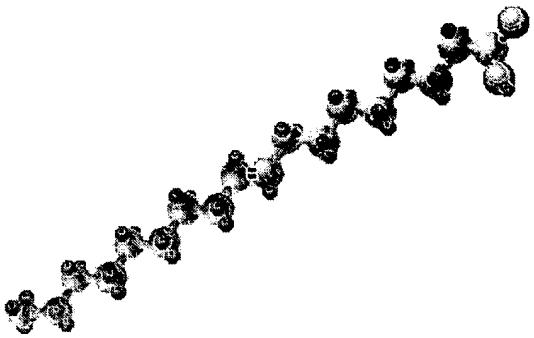


Butyric Acid

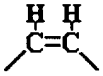
Butyric acid (butanoic acid) is one of the saturated short-chain fatty acids responsible for the characteristic flavor of butter. This image is a detailed structural formula explicitly showing four bonds for every carbon atom and can also be represented as the equivalent line formulas:

Fatty Acid Configurations

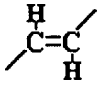
Cis-9-octadecenoic acid
(Oleic acid)



Trans-9-octadecenoic acid
(Elaidic acid)



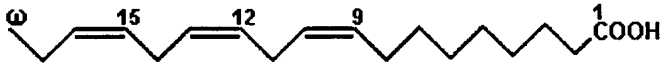
Cis
Configuration



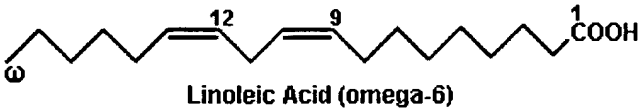
Trans
Configuration

What are Omega-3 and Omega-6 fatty acids?

Omega-3 (ω**3**) and omega-6 (ω**6**) fatty acids are unsaturated "Essential Fatty Acids" (EFAs) that need to be included in the diet because the human metabolism cannot create them from other fatty acids. Since these fatty acids are polyunsaturated, the terms n-3 PUFAs and n-6 PUFAs are applied to omega-3 and omega-6 fatty acids, respectively. These fatty acids use the Greek alphabet ($\alpha,\beta,\gamma,...,\omega$) to identify the location of the double bonds. The "alpha" carbon is the carbon closest to the carboxyl group (carbon number 2), and the "omega" is the last carbon of the chain because omega is the last letter of the Greek alphabet. Linoleic acid is an omega-6 fatty acid because it has a double bond six carbons away from the "omega" carbon. Linoleic acid plays an important role in lowering cholesterol levels. Alpha-linolenic acid is an omega-3 fatty acid because it has a double bond three carbons away from the "omega" carbon. By subtracting the highest double-bond locant in the scientific name from the number of carbons in the fatty acid we can obtain its classification. For arachidonic acid, we subtract 14 from 20 to obtain 6; therefore, it is an omega-6 fatty acid. This type of terminology is sometimes applied to oleic acid which is an omega-9 fatty acid.

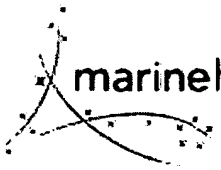


Alpha-Linolenic Acid (omega-3)



Linoleic Acid (omega-6)

In these simplified structural formulas of unsaturated fatty acids, each angle represents a carbon atom. Notice that all the double bonds have the *Cis* configuration.



Omega-3 polyunsaturated fatty acids

Fatty acids are building blocks for eicosanoids, which are precursors for hormones such as prostaglandins and are involved in the formation of cell membranes, blood clotting, wound healing and inflammation. They are termed 'essential' because we need them to live a healthy life but cannot synthesise them.

Fatty acids are based on a chain of linked carbon atoms and are classified as saturated or unsaturated. In a saturated fatty acid there are only single bonds between the carbon atoms — hydrogen atoms take up all other bonds. The term unsaturated means that the fatty acid has at least one carbon-carbon double bond. Polyunsaturated means there are two or more double bonds. The 3 in omega-3 fatty acids (and 6 in omega-6 fatty acids) indicates where the first double bond is in the carbon atom chain.

The two key omega-3 polyunsaturated fatty acids with respect to health benefits are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Unsaturated and polyunsaturated fats have lower melting points and are liquid at room temperature. Typically they are found in vegetable oils and

fish oils, but it is the fish oils in particular that are rich in EPA and

DHA. Omega-3 fatty acids from vegetable sources need to be converted into EPA and DHA in the body before they can be converted into beneficial eicosanoids.

Many benefi to eati

Down

Hea of o revi

Health benefits of omega-3 polyunsaturated fatty acids

The following is an overview of the many health benefits related to eating fish that have been associated with omega-3 polyunsaturated fatty acids. The benefits fit under several broad headings — Heart and Circulation, Moderating inflammatory conditions, Mental health, and Brain development, behaviour and learning abilities. The following section is based on an extensive review of published research.